REMARKS

The present application contains claims 1-88, the status of which is as follows:

(a)   Claims 1-44, 57, 59-65, and 82-88 have been canceled without prejudice.

(b)   Claim 46-53, 55-56, 58, 66-67, and 69-81 were previously presented.

(c)   Claims 45, 54, and 68 have been currently amended.

Claim Objections

The Examiner objected to claims 68-69 due to the term "said roughness" having insufficient antecedent basis. Claim 68 has been amended to depend from claim 67, which recites "a roughness," and claim 69 depends from claim 68. Therefore, the Applicant submits that the Examiner's objection to claims 68-69 has been overcome by the amendment to claim 68.

Claim Rejections Under 35 U.S.C. 101

The Examiner rejected claims 45 and 54, and the claims that depend from these claims, under 35 U.S.C. 101. Claims 45 and 54 have been amended to recite "generating an output on an output device" in response to identifying roughness. These amendments find support in the following portion of the specification:

[0063] Additionally and preferably, the computing and control system 22 also comprises an arteriosclerotic index determiner 22e, using the blood vessel internal surface roughness to determine the level of arteriosclerosis in the blood vessel being imaged. Additionally, the arteriosclerotic index determiner may preferably utilize the roughness in order to ascertain the arteriosclerotic condition of blood vessels elsewhere in the subject's body, as explained hereinabove.

[0064] It is to be understood that the above-described modules used for the analysis within the computing and control system 22, are only one preferred combination for executing the necessary vascular analysis of the present application, and that other combinations which achieve the desired vascular analysis can also be used for executing the

present invention.

[0065] **After generation of this output data, they are preferably directed to a display monitor 24 and/or a printer 26.**

The Applicant submits that the amendments to claims 45 and 54 overcome the Examiner's rejections under 35 U.S.C. 101, of claims 45 and 54, and the claims that depend from these claims.

Claim Rejections Under 35 U.S.C. 103

The Examiner rejected all of the pending claims under 35 U.S.C. 103, over PCT Publication WO 99/63882 to Grinvald ("Grinvald '99") in view of "Carotid bifurcation atherosclerosis: Quantitative Correlation of Plaque Localization with Flow Velocity Profiles and Wall Shear Stress," by Zarins et al., 1983 ("Zarins"), and, in the case of some claims, further in view of additional references.

Claim 45 of the present application recites "utilizing said at least one flow characteristic **for identifying** roughness on an inner wall of said at least one optically accessible blood vessel." (The other independent claims recite similar limitations.) Figs. 3A-F of the present application, for example, show the effect that respective shapes of roughness (Figs. 3A-C) have on the flow characteristics of the erythrocytes:

FIG. 3A

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FIG. 3D

FIG. 3B

44

FIG. 3E

FIG. 3C

FIG. 3F
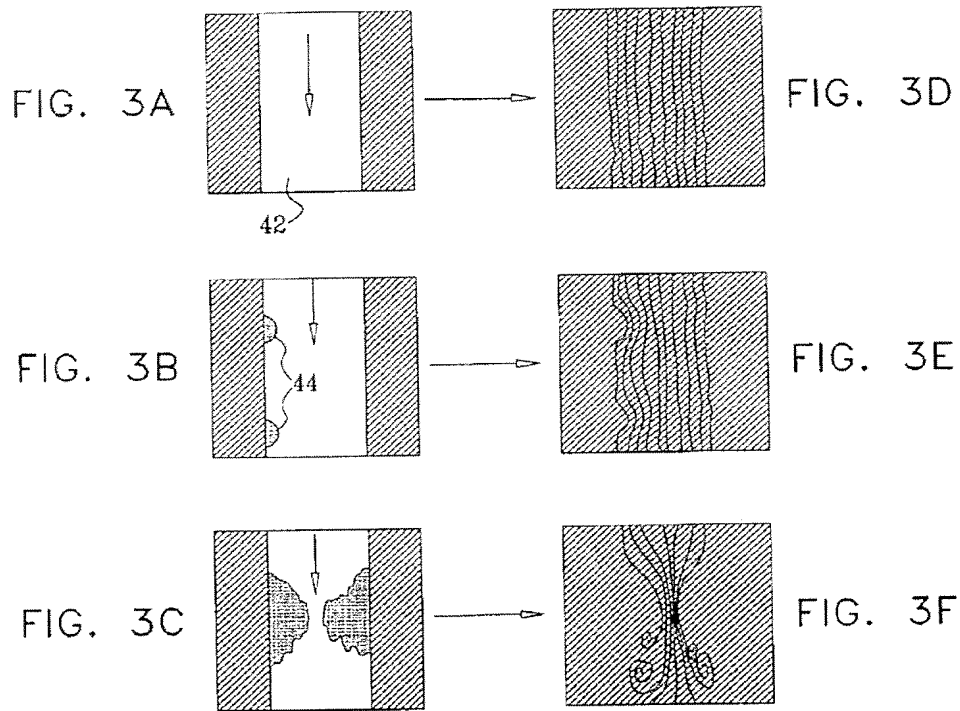
Zarins describes a study in which carotid bifurcations, which were excised at autopsy from healthy subjects, were imaged and analyzed to assess irregularities of lumen contours. **Separately,** artificial, physical models of normal carotid bifurcations were constructed, and velocity profile measurements were taken of a fluid flowing through the models. Wall shear stress along the models was determined based on the measured velocity profiles. The Zarins study concluded that: (a) plaque formation and other pathological phenomena at the carotid bifurcation, as determined based on the images of the autopsied carotid bifurcations, is associated with, i.e., is caused by: (b) hemodynamic variations related to the bifurcation geometry, as determined by the velocity profile measurements of the bifurcation models.

Before initiating the substance of responding to the office action, the Applicant notes that it appears that the Examiner did not understand Zarins as describing his experiment in this manner. It appears that the Examiner thought that Zarins was actually using blood flow measurements to measure flow characteristics that arise from roughening of the blood vessel wall. In fact, Zarins made all of his flow measurements in physical models of blood vessels, in which

any interesting flow characteristics measured were due to the overall shape of the blood vessels, and **not** due to roughness of the blood vessel wall (as presently claimed). As noted in Zarins' Discussion section on p. 511, "By comparing [(a)] the location of non-stenosing intimal disease in human bifurcations with [(b)] flow field distribution ... in anatomically accurate models of the entire bifurcation, we were able to associate atherogenesis with hemodynamic variations related mainly to bifurcation geometry at several levels ..."

The Applicant now provides a table including the Examiner's comments with respect to Zarins, and the Applicant's response.

Examiner's comments from paragraph 4 of the office action	Applicant's response
However, they [Grinvald '99] do not specifically disclose that their method includes the step of utilizing said at least one flow characteristic for identifying roughness on an inner wall of said at least one optically accessible blood vessel. Further, they do not specifically disclose that their method includes the step of utilizing said identifying of said roughness on said inner wall of said at least one optically accessible blood vessel in order to determine a level of arteriosclerosis in the subject ...	Applicant agrees.
Zarins et al. disclose a study *relating* the axial and circumferential distribution of early, asymptomatic, nonstenosing, intimal lesions to flow patterns, flow velocity profiles, and shear stresses ... [emphasis added]	The Applicant respectfully submits that the Examiner's intent in using the word "relating" does not reflect the *relation* that Zarins described. In particular, Zarins' findings indicate that flow patterns etc. **in glass or plexiglass models of a blood vessel** are related to intimal thickening and atherosclerotic plaque formation **identified in autopsy blood vessel specimens.** Thus, Zarins was **not** using flow measurement to identify wall

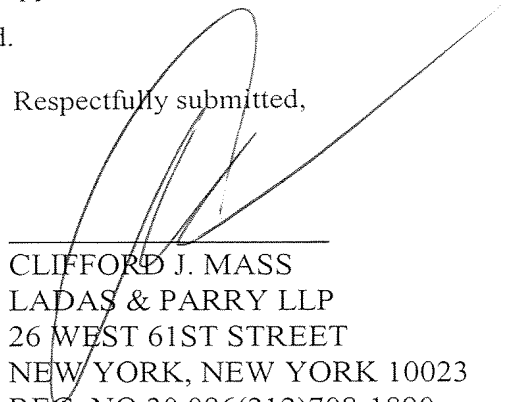|	
	roughening in blood vessels, as apparently considered by the Examiner in making the obviousness rejection. Instead, Zarins identified flow characteristics in artificial physical models of a blood vessel to identify what flow characteristics lead to intimal thickening etc.
They disclose that their findings indicate that regions of reduced wall shear stress, flow separation, flow reversal, and departure from axial flow are <u>associated with</u> maximal intimal thickening and atherosclerotic plaque formation, and regions where flow is axial and unidirectional, and flow velocities and wall shear stresses are high, tend to be spared. [emphasis added]	The Applicant respectfully submits that the Examiner's intent in using the words "associated with" does not reflect the association that Zarins described. In particular, Zarins' findings indicate that regions of reduced wall shear stress etc. **in glass or plexiglass models of a blood vessel** are associated with intimal thickening and atherosclerotic plaque formation **identified in autopsy blood vessel specimens.** Thus, Zarins was <u>not</u> using flow measurement to identify wall roughening in blood vessels, as apparently considered by the Examiner in making the obviousness rejection. Instead, Zarins identified flow characteristics in artificial physical models of a blood vessel to identify what flow characteristics lead to intimal thickening etc.
At the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the invention of Grinvald et al. to include a wall analyzer to perform the step of utilizing at least one flow characteristic (i.e., flow direction, flow rate) for identifying roughness on an inner wall of said at least one optically accessible blood vessel, as Zarins	The Applicant respectfully submits that, as described hereinabove, the Examiner's characterization of Zarins is not correct. The Examiner in this passage is stating, in essence, that it would have been obvious to modify the invention of Grinvald to do "X," where "X" is presumably described in Zarins. As described above, however,

teaches that flow characteristics (i.e., flow direction, flow rate), are indicators of atherosclerotic plaque formation (i.e., roughness on inner wall of blood vessel).	Zarins does not perform the step of utilizing at least one flow characteristic for identifying roughness on an inner wall of an optically accessible blood vessel. On the contrary, Zarins utilizes flow characteristics measured in artificial physical models of blood vessels to identify sites where lesions would be likely to form in real blood vessels.
...Zarins teaches that flow characteristics (i.e., flow direction, flow rate), are indicators of atherosclerotic plaque formation (i.e., roughness on inner wall of blood vessel).	Zarins teaches that flow characteristics are indicators of **future** atherosclerotic plaque formation (i.e., roughness on inner wall of blood vessel). Zarins does not assess how measured flow characteristics are caused by roughness.

In view of the arguments made herein, the Applicant submits that independent claims 45, 54, and 66 are patentable over Grinvald '99 in view of Zarins.

The remaining pending claims, being dependent from the aforementioned claims, and, therefore, of narrower scope than the aforementioned claims, are also patentable over the art of record.

The Applicant believes the amendments and remarks presented hereinabove to be fully responsive to all of the grounds of rejection and objection raised by the Examiner. In view of these amendments and remarks, the Applicant respectfully submits that all of the claims in the present application are now in order for allowance. Notice to this effect is respectfully requested.

Respectfully submitted,

CLIFFORD J. MASS
LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NEW YORK 10023
REG. NO.30,086(212)708-1890

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